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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/980,559	05/14/2002	Masayuki Yanagi	2026-4302US	8862

7590 03/25/2005

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EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 03/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/980,559	YANAGI ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-11 ans 37-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-11 and 37-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

4/C

DETAILED ACTION

RCE

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/27/2004 has been entered. The RCE follows:

Response to Amendment

This is a response to the amendment, paper No. 13, filed 12/27/04. Claim 3 has been amended. Claims 1 and 12-36 have been canceled. Claims 2-11 and 37-39 are pending. are pending before the examiner.

Please note any ground of rejection(s) that has not been repeated is removed. Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Declaration under 37 CFR 1.132

The Declaration under 37 CFR 1.132 filed on December 27, 2004 has been acknowledged.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 2, 3-7 and 37 are still rejected under 35 U.S.C. 102(b) as being anticipated by Okamoto et al. (EP 532 167A2) or Kokamoto et al. (US Patent No. 5/428,145A).

3. In response to the previous Office Action, Applicants filed a Declaration under 37 CFR 1.132. In the declaration, Dr. Raymond states that by using BLASTX analyses, that the amino

acid sequence disclosed by Okmato has 97.8% homology to the claimed sequence of SEQ ID NO: 2 and the nucleic acid sequence has 95.9% identity to the claimed SEQ ID NO: 1. However, it is insufficient to overcome the rejection. Because according to the sequence analysis, the overall query match for the claimed DNA sequence of SEQ ID NO: 1 with the DNA sequence disclosed by Okamoto in EF532167A2 or US Patent No. 5/428,145A has 96% homology. That different is 4% that is < 4.1%. The amino acid sequence encoded by the HCV polynucleotide disclosed by Okamoto in EF 532167A2 or US Patent No. 5/428,145A exhibits 98.16% homology to the claimed sequence of SEQ ID NO: 2. That different is 1.84%, which is <4.1% (Please see the sequence search report).

4. Okamoto et al. also teach that the isolated HCV-J6 RNA sample is prepared in a composition comprising Tris chloride buffer (50 mM, pH 8.0) with 200 mM NaCl etc, which is a pharmaceutical accepted diluent and exciepinet (See line 40-44 on page 5). Therefore, it meets the limitations of claimed nucleotide sequence has less than 4.1% to the SEQ ID NO: 1 at the nucleic acid level and 2.2% to the SEQ ID NO: 2 at the amino acid level.

5. Applicants further argue that one of the inventor, Dr. Yanagi once published a paper in Virology in 1999 that teaches the 3' UTR consists of 3 regions: a short variable region, a polypyrimidine tract of variable length, and a highly conserved terminal region of approximately 100 nts. The polypyrimidine tract and the conserved region of the 3' UTR are essential for infectivity in vivo. Whereas, this feature has not taught by any reference cited by the examiner.

6. In response to this argument that the references fail to show certain features of applicant's invention; however, it is noted that the features upon which applicant relies (i.e., 3' 100 nts of polypyrimidine trac) are not recited in the rejected claim(s).

7. Hence, the claimed invention is still anticipated by the cited reference.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 2, 3-11 and 37 are still rejected under 35 U.S.C. 103(a) as being unpatentable over Kokamoto et al. (US Patent No. 5/428,145A) and Yoo et al. (J. Virol. 1995, Vol. 69, No. 1, pp. 32-38).

10. Claimed invention is drawn to an isolated nucleotide molecule encoding a HCV genome, a RNA transcript or a host cell transfected with said RNA or DNA, wherein the DNA sequence has less than 4.1% different to the claimed SEQ ID NO: 1 at the nucleic acid level, wherein the DNA molecule encodes the amino acids that has less than 2.2% homology to the SEQ ID NO: 2 at the amino acid level.

11. In response to the previous Office Action, Applicants filed a Declaration under 37 CFR 1.132. In the declaration, Dr. Raymond states that by using BLASTX analyses, that the amino acid sequence disclosed by Okmato has 97.8% homology to the claimed sequence of SEQ ID NO: 2 and the nucleic acid sequence has 95.9% identity to the claimed SEQ ID NO: 1. However, it is insufficient to overcome the rejection. Because according to the sequence analysis, the overall query match for the claimed DNA sequence of SEQ ID NO: 1 with the DNA sequence disclosed by Okamoto in EF532167A2 or US Patent No. 5/428,145A has 96% homology. That different is 4% that is < 4.1%. The amino acid sequence encoded by the HCV polynucleotide disclosed by Okamoto in EF 532167A2 or US Patent No. 5/428,145A exhibits 98.16% homology to the claimed sequence of SEQ ID NO: 2. That different is 1.84%, which is <4.1% (Please see the sequence search report).

12. Okamoto et al. also teach that the isolated HCV-J6 RNA sample is prepared in a composition comprising Tris chloride buffer (50 mM, pH 8.0) with 200 mM NaCl etc, which is a pharmaceutical accepted diluent and exciepinet (See line 40-44 on page 5). Therefore, it meets the limitations of claimed nucleotide sequence has less than 4.1% to the SEQ ID NO: 1 at the nucleic acid level and 2.2% to the SEQ ID NO: 2 at the amino acid level (See lines 40-51 on col. 12 and claims 1-6). While Okamoto et al. do not explicitly disclose a host cell transfected with such nucleic acid molecule, they teach that the polynucleotide with those identified sequences can be used to express polypeptide in host cells such as Escherichia coli by the well-know

genetic engineering technique (See lines 46-48 on page 12). Yoo et al. explicitly teach a method for using the Huh7 cells to establish the long-term culture persistently express HCV by transfecting the cells with the HCV RNA transcript and establish the cell line harboring the HCV RNA or DNA molecule (See entire document, especially the first col. of page 33).

13. Applicants further argue that one of the inventor, Dr. Yanagi once published a paper in Virology in 1999 that teaches the 3' UTR consists of 3 regions: a short variable region, a polypyrimidine tract of variable length, and a highly conserved terminal region of approximately 100 nts. The polypyrimidine tract and the conserved region of the 3' UTR are essential for infectivity in vivo. Whereas, this feature has not taught by any reference cited by the examiner.

14. In response to this argument that the references fail to show certain features of applicant's invention; Applicants are reminded that the features upon which applicant relies (i.e., 3' 100 nts of polypyrimidine trac) are not recited in the rejected claim(s).

15. Therefore, it would still have been obvious for a person with ordinary skill in the art to be motivated by the disclosed prior art to express the HCV virus in view of the technique taught by Yoo et al. and establish a host cell line harboring the isolated HCV nucleic acid molecule. Hence the rejection maintained.

New Ground of Objection and Rejection.

New matter objection

The amendment filed on 12/27/2004 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: (1). In claim 2, line 5: "<2.2%" and (2). Claim 3, lines 3-4, "from nucleotide 341 to 9439, which corresponds to the ORF, by <4.1% at the nucleotide level."

Applicant is required to cancel the new matter in the reply to this Office Action.

New matter rejection under - 35 USC § 112

16. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

17. Claims 2 and 3 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the amendment of claim 2, line 5: "<2.2%" and claim 3, lines 3-4, "from nucleotide 341 to 9439, which corresponds to the ORF, by <4.1% at the nucleotide level." are not disclosed in specification as it was original file

18. Applicants asserted that the support for these amendments could be found in page 40 Table 2 and Fig. 2. The Table 2 and Fig. 2 disclosed in the specification have been carefully reviewed. The Fig. 2 does not tell anything about the precise percentages about the amended claims. Table 2 only teaches that the differences between the nucleic acid sequence and amino acid sequence between JC-6 strain disclosed by Okamoto et al. and the claimed HC-$J6_{CH}$. However, the claims are directed to the differences about the nucleic acid sequence or amino acid sequence between the broad claimed any or all nucleic acid sequences with the claimed defined sequence of SEQ ID NO: 1 or 2. The SEQ ID NO: 1 or SEQ ID NO: 2 are not the nucleic acid sequence and amino acid sequence of Okamoto. Therefore, this is a new matter.

19. Claims 2 and 3 are also rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, applicants do not have the possession for having any or all nucleic acid molecules that encodes an amino acid sequence that different from that of SEQ ID NO: 2 by <2.2% at the amino acid level or that differs from that of SEQ ID NO: 1 from nucleotide 341 to 9439, which corresponds to the ORF by <4.1 at the nucleic acid level.

20. The written description requirement under Section 112, first paragraph, sets forth that the claimed subject matter must be supported by an adequate written description that is sufficient to enable anyone skilled in the art to make and use the invention. The courts have concluded that

the specification must demonstrate that the inventors had possession of the claimed invention as of the filing date relied upon.

21. In the instant case, the specification only teaches that an isolated nucleic acid molecule of SEQ ID NO: 1 that encodes a amino acid sequence SEQ ID NO: 2 of HCV $JH6_{CH}$ strain. However, the claims encompass the scope of a any or all protein comprising any or all fragment with less than 2.2% at nucleic acid sequence level or SEQ ID NO: 1 or less than 4.1% of amino acid level of SEQ ID NO: 2. The claims do not require that the claimed fragment possess any particular distinguished feature, or conserved sequence structure. Therefore, the claims are drawn to genus proteins that are not defined by any distinct structural characteristics or sequence identity.

22. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguished identified characteristics of the genus protein. The factors to be considered include the physical and/or chemical properties, functional characteristics, structural/functional correlation, and methods of making the claimed product or any combination thereof.

23. Vas-Cath. V. Makurkar, 19USPQ2d 111, clearly states "applicant must convey with reasonable clarity to those skilled in the art, as of the filling date sough, he or she was in possession of the invention. The invention is, for purpose of the 'written description' inquiry, whatever is now claimed." (see page 1117). The specification should "clearly allow person of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). Moreover, to be in the possession of any claimed invention, the applicants must show that a significance of conception and reduction to practice was reached before the application was filed. This concept is further addressed by the court in Fiers v. Sugano where it was emphasized that "[c]onception is a question of law, reviewed de novo on appeal, and if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, regardless of complexity or simplicity of method of isolation.

24. As discussed above, the skilled artisan cannot envision the detail chemical structure of encompassed genus of proteins comprising any fragment of less than 2.2% of SEQ ID NO: 1 or les than 4.1 % to SEQ ID NO 2. An adequate written description requires more than a mere

statement of what it is or what it may be or a reference to a potential method of isolating it. The compound itself is required. (See Fier v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 UQPQ2d 1016.

25. Therefore, only isolated nucleic acid molecule of SEQ ID NO: 1 that encodes the amino acid sequence of SEQ ID NO: 2 meets the written description provision of 35 U.S.C § 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C § 112 is severable from its enablement provision (See page 1115).

26. To this context, the generic sequence but not the sequence of SEQ ID NO: 1 or SEQ ID NO: 2 are rejected under the written description 112 1st paragraph in the claims.

Conclusion

Claims 38 and 39 are deem free of art rejection. However, they are not in condition for allowance because they depend on the rejected claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 571-272-0904. The examiner can normally be reached on 7:00 am to 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bao Qun Li

03/19/2005